1,185,039

PATENT SPECIFICATION

NO DRAWINGS

1,185,039

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Date of filing Complete Specification: 10 March, 1967.

Date of Application (No. 14270/66): 31 March, 1966.

Complete Specification Published: 18 March, 1970.

Index at acceptance:—C2 C(2D6, 2D7, 2D14, 3A10E3C4, 3A10E5F1E, 3A10E5F2A, 3A10E5F3B, 3A10E5F3D, 3C10, 200, 215, 22Y, 220, 226, 247, 25Y, 250, 252, 253, 28X, 30Y, 31Y, 313, 314, 32Y, 321, 322, 323, 332, 337, 338, 358, 366, 368, 491, 620, 628, 658, 661, 668, 67X, 670, 671, 678, 688, 79Y, 791, 171—27X—289, 175—193—286, LS, LT, LW, LZ); A5 E(1C4B2, 1C4B3, 1C4B4, 1C17)

International Classification:—C 07 d 51/42

COMPLETE SPECIFICATION

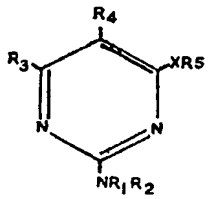
Pyrimidine Derivatives and Compositions containing them

We, IMPERIAL CHEMICAL INDUSTRIES LIMITED, a British Company of Imperial Chemical House, Millbank, London, S.W.1, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to new pyrimidine derivatives, to processes for making them, to pesticidally active compositions containing them and to methods for combating pests.

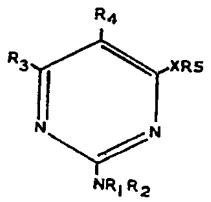
Accordingly this invention provides, as new compounds, 2-amino pyrimidines, bearing in the 6-position a carboxyl- or sulphonyl-esterified hydroxy or mercapto group; or salts thereof.

More particularly the invention provides a pyrimidine derivative having the formula:—



or a salt thereof, wherein R_1 and R_2 represent atoms of hydrogen, substituted or unsubstituted hydrocarbon groups, or together with the adjacent N-atom form a heterocyclic ring which may contain one or more additional hetero- atoms; R_3 and R_4 represent atoms of hydrogen or halogen, substituted or unsubstituted hydrocarbon groups, or nitro groups; X represents an atom of oxygen or sulphur; and R_5 is a carbonyl or sulphonyl group bearing directly, or through an oxygen or sulphur atom, a substituted or unsubstituted hydrocarbon group, or a heterocyclic group.

More specifically, the invention provides a pyrimidine derivative having the formula:—



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or a salt thereof, wherein R_1 and R_2 represent hydrogen atoms, lower alkyl radicals, halophenyl radicals, or together with the adjacent nitrogen atom form a piperidino radical, a morpholino radical, or a 1-methylpiperazin-4-yl radical; R_3 represents a hydrogen atom, a lower alkyl radical or a phenyl radical; R_4 represents an atom of hydrogen or bromine, a lower alkyl, lower alkenyl, or benzyl radical, or a nitro group; X represents an atom of oxygen or sulphur; and R_5 is a carbonyl or sulphonyl group bearing directly, or through an atom of oxygen or sulphur, a lower alkyl radical, a lower alkenyl radical, a phenyl radical or a nitro-, halo-, lower alkyl- substituted phenyl radical, a piperidino radical, a furyl radical or a styryl radical.

Preferred pyrimidine derivatives according to this invention are those having the general formula set out above wherein R_1 and R_2 represent hydrogen, or lower alkyl radicals; R_3 represents hydrogen, a lower alkyl radical or a phenyl radical; R_4 represents an atom of bromine, a lower alkyl, lower alkenyl or benzyl radical, and R_5 is a carbonyl or sulphonyl group bearing a lower alkyl radical, a lower alkoxy radical, a lower alkylthio radical, a phenyl radical or a nitro-, lower alkyl- or halo-substituted phenyl radical, a phenylthio radical, an alkenyl radical, an arelkenyl radical or a piperidino or furyl radical; or a salt thereof.

Particular pesticidally active pyrimidine derivatives according to the invention are those wherein R_1 and R_2 are hydrogen or lower alkyl radicals; R_3 is a lower alkyl radical; R_4 is a lower alkyl radical having 2 to 6 carbon atoms; and R_5 is a carbonyl or sulphonyl group bearing a lower alkyl radical, a lower alkoxy radical, a phenyl radical or a styryl radical.

Preferred particularly pesticidally active pyrimidine derivatives are those wherein R_1 and R_2 are both methyl radicals or R_1 is hydrogen and R_2 is an ethyl radical; R_3 is a methyl radical; R_4 is a butyl or amyl radical; X is an atom of oxygen; and R_5 is a lower alkyl, lower alkoxy or phenyl radical.

By the terms "lower alkyl," "lower alkenyl" and "lower alkoxy" in this specification and claims are intended radicals containing from one to six carbon atoms.

Specific pyrimidine derivatives of the invention which have been found to be particularly useful are listed in the Table I below. The headings to the columns of the Table correspond to the substituent groups on the pyrimidine ring in the general formula set out above.

TABLE I

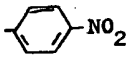
COMPOUND NO.	NR_1R_2	R_3	R_4	XR_5
1	$-N(CH_3)_2$	CH_3	nC_3H_7	
2	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-CO-C_6H_5$
3	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-SO_2-C_6H_5$
4	$-N(CH_3)_2$	CH_3	$-CH_2-CH=CH_2$	$O-CO-C_6H_4NO_2(p)$
5	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-SO_2-C_6H_4-CH_3(p)$
6	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-SO_2-CH_3$

TABLE I continued

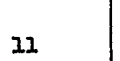
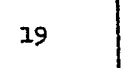
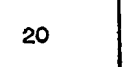
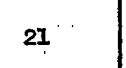
7	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-\overset{O}{\overset{\|}{C}}-S-C_6H_5$
8	$-N(CH_3)_2$	CH_3	nC_5H_{11}	$O-CO-C_6H_5$
9	$-N(CH_3)_2$	CH_3	nC_3H_7	$-O-CO-C_6H_4-Cl$ (m)
10	$-N(CH_3)_2$	CH_3	nC_4H_9	$O-CO-C_6H_5$
11		CH_3	nC_4H_9	$O-SO_2-CH_3$
12	$-N(CH_3)_2$	CH_3	nC_5H_{11}	$O-SO_2-CH_3$
13	$-N(CH_3)_2$	CH_3	nC_4H_9	$O-SO_2-CH_3$
14	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-CO-CH_3$
15	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-SO_2-C_6H_4-NO_2$(m)
16	$-N(CH_3)_2$	CH_3	nC_3H_7	
17	$-N(CH_3)_2$	CH_3	H	$O-SO_2-CH_3$
18	$-N(CH_3)_2$	CH_3	nC_4H_9	$S-\overset{O}{\overset{\|}{C}}-OC_2H_5$
19		CH_3	H	$O-SO_2CH_3$
20			H	$O-SO_2CH_3$
21		CH_3	H	$O-SO_2-C_2H_5$
22	$-N(CH_3)_2$	CH_3	C_2H_5	$O-CO-$ 

TABLE I continued

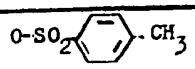
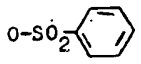
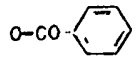
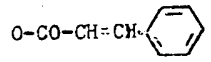
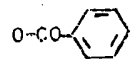
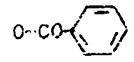
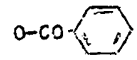
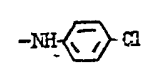
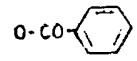
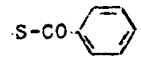
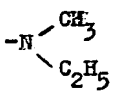
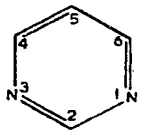
23		CH_3	H	
24		CH_3	H	
25	$-N(CH_3)_2$	CH_3	$SecC_5H_{11}$	
26	$-N(CH_3)_2$	CH_3	nC_3H_7	$O-CO-CH=CH-CH_3$
27	$-N(CH_3)_2$	CH_3	nC_3H_7	
28	$-NH-C_2H_5$	CH_3	nC_4H_9	
29		CH_3	H	
30	$-N(CH_3)_2$	H	H	$O-SO_2-CH_3$
31	$-N(CH_3)_2$	CH_3	Br	
32		CH_3	H	
33	$-N(CH_3)_2$	CH_3	nC_4H_9	
34	$-N(CH_3)_2$	CH_3	CH_3	$O-CO-OC_2H_5$
35	$-N(CH_3)_2$	CH_3	CH_3	$O-CO-OnC_4H_9$
36	$-N(CH_3)_2$	CH_3	CH_3	$S-CO-OnC_3H_7$
37	$-N(CH_3)_2$	CH_3	nC_3H_7	$S-CO-OnC_3H_7$
38	$-N(CH_3)_2$	CH_3	nC_4H_9	$O-CO-OC_2H_5$
39	$-N(CH_3)_2$	CH_3	nC_4H_9	$O-CO-OnC_3H_7$

TABLE I continued

40	$-N(CH_3)_2$	CH_3	nC_4H_9	$O-CO-OnC_4H_9$
41	$-N(CH_3)_2$	CH_3	nC_4H_9	$S-CO-OnC_3H_7$
42		nC_3H_7	H	$O-CO-C_6H_5$
43	$-N(CH_3)_2$	nC_3H_7	C_2H_5	$O-CO-C_6H_5$
44		CH_3	nC_4H_9	$O-CO-C_6H_5$
45	$-NH_2$		H	$O-CO-C_6H_5$
46	$-N(CH_3)_2$	CH_3		$O-CO-C_6H_5$
47	$-N(CH_3)_2$	CH_3	H	
48	$-N(CH_3)_2$	H	NO_2	$O-CO-C_6H_5$

Compound No. 14 in Table I above is readily hydrolysed by water.
In this specification the numbering of the pyrimidine ring is as follows:—

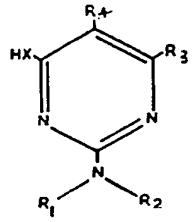


It may be noted that the 4- and 6- positions are equivalent.

As suitable salts of the pyrimidine derivatives of this invention there may be mentioned, for example, the hydrochlorides.

According to a further feature of the invention, we provide the novel pyrimidine derivatives listed in Table I herein above.

The invention also provides a process for making the pyrimidine derivatives of this invention which comprises reacting a compound of the formula:—



wherein R_1, R_2, R_3, R_4 and X have any of the meanings stated above with an acyl or sulphonyl halide of the formula:—

$$R_5 \text{ —— Hal}$$

wherein R_5 has any of the meanings stated above and Hal represents a halogen atom, under conditions where the hydrogen halide which is formed is removed as it is produced.

The foregoing process is preferably carried out in the presence of a diluent as a reaction medium and suitable diluents include substances acting as solvents for either or both of the reactants. Suitable solvents are organic solvents, for example benzene, toluene, lower aliphatic ketones such as methyl ethyl ketone, or acetonitrile. A particularly preferred solvent is ethyl acetate.

The hydrogen halide produced during the reaction may be removed, for example, by carrying out the reaction in the presence of an acid acceptor. Suitable acid acceptors are bases or a salt of a strong base and a weak acid. If a base is used it may be, for example, a tertiary amine. Preferred tertiary amines are triethylamine and pyridine. The base may also be, for example, an alkali or alkaline earth metal hydroxide, for example, sodium hydroxide. If a salt of a strong base and a weak acid is used as the acid acceptor then a suitable salt is an alkali or alkaline earth metal carbonate. A preferred such salt is potassium carbonate.

The invention further provides a process for making the pyrimidine derivatives of the invention which comprises reactig the appropriate acyl or sulphonyl halide with a metallic salt of the appropriate 6-hydroxy- or 6-mercapto- pyrimidine, if necessary in the presence of a solvent to facilitate the reaction. Suitable solvents include those recited above.

The pyrimidine derivatives of the invention possess activity against a wide variety of fungal diseases including the following specific diseases:—

Puccinia recondita (rust) on wheat
Phytophthora infestans (late blight) on tomatoes
Sphaerotheca fuliginea (powdery mildew) on cucumber
Erysiphe graminis (powdery mildew) on wheat and barley
Podosphaera leucotricha (powdery mildew) on apple
Uncinula necator (powdery mildew) on vine
Plasmopara viticola (downy mildew) on vine
Piricularia oryzae (blast) on rice
Venturia inaequalis (scab) on apple
Pythium ultimum (seedling rot) on peas
Fusarium culmorum (stem rot) on wheat

The compounds of the present invention are toxic towards a variety of insect pests including mosquito larvae (*Aedes aegypti*), black aphids (*Aphis fabae*), green aphids (*Macrosiphum pisi*), red spider mites (*Tetranychus telarius*), mustard beetles (*Phaedon cochleariae*), and root knot nematodes (*Meloidogyne incognita*).

A particularly useful feature of the activity of the pyrimidine derivatives of the invention is their systemic effect, that is to say, their ability to move throughout the plant to reach any part thereof bearing a fungal infection and/or insect infestation and to combat the same.

We have found that the pesticidal activity of the novel pyrimidine derivatives of the invention is decreased if both R_3 and R_4 are hydrogen, or if R_4 is an alkyl radical containing more than 7 carbon atoms.

A particularly useful pyrimidine derivative is that in which R_1 and R_2 are both methyl, R_3 is methyl, R_4 is nC_4H_9, and XR_5 is $O—CO—C_6H_5$, that is Compound No. 10 in the foregoing Table I.

According to a preferred embodiment of the invention, we accordingly provide fungicidal compositions comprising as active ingredient 2-dimethylamino-4-methyl-5-n-butyl-6-phenylcarbonyloxy-pyrimidine.

Other particularly useful pyrimidine derivatives are the compounds numbered 8, 10, 12, 13, 27, 28, 39, 40 and 41 in Table I above.

The pesticidally active pyrimidine derivatives of this invention are used to combat plant pests in a number of ways. Thus they can be applied to the foliage of an infected plant, to seed or to the soil in which plants are growing or to be planted.

In a further aspect, therefore, the invention includes a method for the combating of undesired fungal infections in plants which comprises applying to the locus of the plant, a pyrimidine derivative as hereinbefore defined or a composition as hereinafter defined.

In a yet further aspect the invention includes a method of cambating insect infestations in plants which comprises applying to the locus of the plant an insecticidally active pyrimidine derivative as hereinbefore defined or a composition as hereinafter defined.

In yet a further aspect the invention includes a method for treating agricultural soil to combat pests on plants comprising applying to the soil a pyrimidine derivative as hereinbefore defined or a composition as hereinafter defined.

The invention includes, therefore, a method of combating plant pathogens which comprises applying to a plant, or to seed thereof, a pyrimidine derivative as hereinbefore defined or a composition as hereinafter defined.

The pyrimidine derivatives of this invention are preferably used in the form of compositions and these compositions may be used for agricultural and horticultural purposes. The type of composition used in any instance will depend upon the particular purpose for which it is to be used.

The compositions may be in the form of dusting powders or granules wherein the active ingredient is mixed with a solid diluent or carrier. Suitable solid diluents or carriers may be, for example, kaolin, bentonite, kieselguhr, dolomite, calcium carbonate, talc, powdered magnesia, Fuller's earth, gypsum, Hewitt's earth, diatomaceous earth and China clay. Compositions for dressing seed, for example, may comprise an agent assisting the adhesion of the composition to the seed, for example a mineral oil. The compositions may also be in the form of dispersible powders or grains comprising, in addition to the active ingredient, a wetting agent to facilitate the dispersion of the powder or grains in liquids. Such powders or grains may include fillers, suspending agents and the like.

The compositions may also be in the form of liquid preparations to be used as dips or sprays which are generally aqueous dispersions or emulsions containing the active ingredient in the presence of one or more wetting agents, dispersing agents, emulsifying agents or suspending agents.

Wetting agents, dispersing agents and emulsifying agents may be of the cationic, anionic or non-ionic type. Suitable agents of the cationic type include, for example, quaternary ammonium compounds, for example, cetyltrimethylammonium bromide. Suitable agents of the anionic type include, for example, soaps, salts of aliphatic monoesters of sulphuric acid, for example sodium lauryl sulphate, salts of sulphonated aromatic compounds, for example sodium dodecylbenzenesulphonate, sodium, calcium or ammonium lignosulphonate, butyl-naphthalene sulphonate, and a mixture of the sodium salts of diisopropyl- and triisopropyl- naphthalene sulphonic acids. Suitable agents of the non-ionic type include, for example, the condensation products of ethylene oxide with fatty alcohols such as oleyl alcohol or cetyl alcohol, or with alkyl phenols such as octylphenol, nonylphenol and octylcresol. Other non-ionic agents are the partial esters derived from long chain fatty acids and hexitol anhydrides, the condensation products of the said partial esters with ethylene oxide, and the lecithins.

Suitable suspending agents are, for example, hydrophilic colloids, for example polyvinylpyrrolidone and sodium carboxymethylcellulose, and the vegetable gums, for example gum acacia and gum tragacanth.

The aqueous dispersions or emulsions may be prepared by dissolving the active ingredient or ingredients in an organic solvent which may contain one or more wetting, dipersing or emulsifying agents and then adding the mixture so obtained to water which may likewise contain one or more wetting, dispersing or emulsifying agents. Suitable organic solvents are ethylene dichloride, isopropyl alcohol, propylene glycol, diacetone alcohol, toluene, kerosene, methylnaphthalene, xylenes and trichloroethylene.

The compositions to be used as sprays may also be in the form of aerosols wherein the formulation is held in a container under pressure in the presence of a propellant such as fluorotrichloromethane or dichlorodifluoromethane.

By the inclusion of suitable additives, for example for improving the distribution, adhesive power and resistance to rain on treated surfaces, the different compositions can be better adapted for the various uses for which they are intended.

The pyrimidine derivatives may also be conveniently formulated by admixing them with fertilizers. A preferred composition of this type comprises granules of fertiliser material incorporating, for example coated with, a pyrimidine derivative. The fertiliser material may, for example, comprise nitrogen or phosphate-containing substances.

In yet a further aspect of the invention, therefore, we provide a fertiliser composition comprising a pyrimidine derivative as hereinbefore defined.

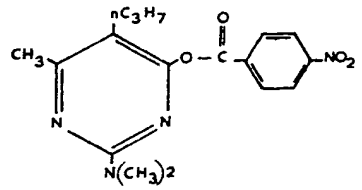
The compositions which are to be used in the form of aqueous dispersions or emulsons are generally supplied in the form of a concentrate containing a high proportion of the active ingredient or ingredients, the said concentrate to be diluted with water before use. These concentrates are often required to withstand storage for prolonged periods and after such storage, to be capable of dilution with water in order to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. The concentrates may conveniently contain from 10—85% by weight of the active ingredient or ingredients and generally from 25—60% by weight of the active ingredient or ingredients. When diluted to form aqueous preparations, such preparations may contain varying amounts of the active ingredient or ingredients depending upon the purpose for which they are to be used, but an aqueous preparation containing between 0.001% and 1.0% by weight of active ingredient or ingredients may be used.

It is to be understood that the biologically active compositions of this invention may comprise, in addition to a pyrimidine derivative, one or more other compounds having biological activity. They may also incorporate one or more stabilising agents, for example epoxides, for example epichlorhydrin.

The invention is illustrated by the following Examples, those numbered 1 to 5 exemplifying methods of preparing the pyrimidine compounds listed in Table I above, while those numbered 6 to 13 are illustrative of compositions containing various of the pyrimidine derivatives as active ingredient. In the latter group all references to percentage amounts of constituent are by weight and are based on the weigth of the compositions as a whole.

EXAMPLE I

2-Dimethylamino-4-methyl - 6 - (4'-nitrophenyl)carbonyloxy-5-n-propylpyrimidine, (Compound No. 1, Table I) having the formula: —



was prepared as follows: 2-dimethylamino-4-methyl-6-hydroxy-5-n-propylpyrimidine (1.95 g., 0.01 mole) was added to a solution of sodium (0.23 g., 0.01 mole) in dry ethanol (25 ml.). The solution was kept at 40°C for 1 hour, the solvent removed in vacuo, and the residue dried by azeotropic distillation with benzene. To the residue was added dry benzene (25 ml.) and freshly prepared p-nitrobenzoyl chloride (2.3 g., 0.012 mole) and the reaction mixture stirred and refluxed for 4 hours. The cooled mixture was shaken with ice-cold 5% aqueous sodium hydroxide solution, washed with water until the washings were neutral, and the benzene layer dried (Na_2SO_4).

Removal of the benzene, followed by removal of last traces of solvent at the oil pump, gave a viscous residue which crystallised on tritruration with petroleum ether. Recrystallisation from ethanol gave a product, m.p. 109°C. (1.8 g., 53%).

Although the above reaction was conducted in benzene, other solvents such as toluene, lower aliphatic ketones such as methyl ethyl ketone, acetonitrile and ethyl acetate were found to be suitable for the purpose. The preferred solvent is ethyl acetate.

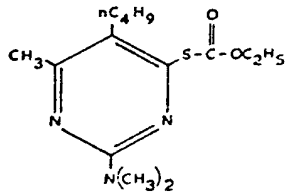
The following compounds were also prepared by the method of Example 1.

Compound No.	Physical Characteristic	Solvent of Crystallisation
2	m.p. 58°	EtOH
3	m.p. 72°	EtOH
4	m.p. 114°	EtOH
5	m.p. 68°	EtOH
6	m.p. 71°	EtOH
7	b.p. 150—155°/0.1 mm	—
8	m.p. 57°	EtOH
9	m.p. 89°	EtOH
10	m.p. 59°	EtOH
11	m.p. 162°	EtOH
13	m.p. 67°	EtOH
14	m.p. 69°	EtOH
15	m.p. 109°	EtOH
16	m.p. 71°	EtOH
17	m.p. 87°	EtOH
22	m.p. 89°	EtOH
23	m.p. 104—105°	MeOH
25	m.p. 63°	EtOH
26	$n_D^{21} = 1.5282$	—
27	m.p. 88°	EtOH

Compound No.	Physical Characteristic	Solvent of Crystallisation
28	m.p. 69—70°	EtOH/H_2O
29	m.p. 120°	EtOH
30	m.p. 76°	EtOH
31	m.p. 128—129°	EtOH
32	m.p. 114—116°	EtOH
42	m.p. 40—46°	EtOH
43	m.p. 62°	EtOH
44	m.p. 45°	*iso*-propyl alcohol
45	m.p. 122—123°	*iso*-propyl alcohol
46	m.p. 92°	EtOH
47	$n_D^{20} = 1.5251$	—
48	m.p. 125—126°	EtOH

EXAMPLE 2

S - (5 - n - Butyl - 2 - dimethylamino - 4 - methyl - 6 - pyrimidyl) O - ethyl-thiolcarbonate (Compound No. 18, Table I) having the formula:—



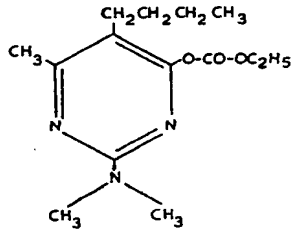
was prepared as follows:— 5-n-Butyl-2-dimethylamino-4-methyl-6-mercapto- pyrimidine (6.75 g.) was dissolved in a solution of sodium hydroxide (1.3 g.) in water (100 ml.). Ethyl chloroformate (3.3 g.) was added and the reaction mixture stirred at room temperature for 3 hours. The product was obtained by extraction with ether. The ether extracts dried with water, dried (Na_2SO_4), and the solvent removed to leave a viscous oil, $n_D^{26} = 1.5444$.

The following compound was also prepared by the method of Example 2, by the use of benzoyl chloride in the place of ethyl chloroformate.

Compound No.	Physical Characteristics
33	b.p. 174—177°/0.12 mm. $n_D^{20} = 1.6008$

EXAMPLE 3

This Example illustrates the preparation of 5-n-butyl-2-dimethylamino-4-ethoxy-carbonyloxy-6-methyl-pyrimidine (Compound No. 38, Table I) having the structure:—



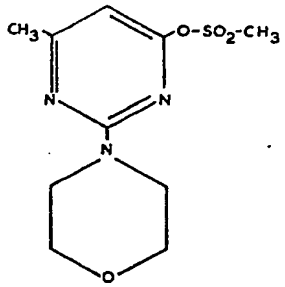
To a solution of 5-n-butyl-2-dimethylamino-4-hydroxy-6-methyl pyrimidine (5.0 g.) in pyridine (100 c.c.) ethylchloroformate (2.9 g.) was added dropwise, and the mixture stirred and kept at ambient temperature for 72 hours. The pyridine was removed from the mixture by evaporation at reduced pressure, and the residual mixture distributed between water and methylene chloride. The aqueous layer was discarded and the methylene chloride solution washed twice with water, then twice with an equal volume of a 4% solution of sodium hydroxide, and finally with water until the washings were neutral. After drying the methylene chloride solution over anhydrous sodium sulphate, and filtering to remove the solid, the methylene chloride was evaporated off and the residual oil distilled. 5-n-butyl-2-dimethylamino-4-ethoxy-carbonyloxy-6-methyl-pyrimidine was obtained as a colourless oil, b.p. 109—110° at 0.01 mm. Hg, $n_D^{22.5} = 1.5034$.

The following compounds were also obtained by the method of Example 3.

Compound No.	b.p.
34	106—109°C/0.01 mm.
35	105°C/0.03 mm.
36	119—120°C/0.05 mm.
37	99—101°C/0.02 mm.
39	118—119°C/0.04 mm.
40	122—123°C/0.01 mm.
41	132—134°C/0.015 mm.

EXAMPLE 4

4-Methyl-6-methylsulphonyloxy-2-morpholino-pyrimidine, (Compound No. 19, Table I) having the formula:—

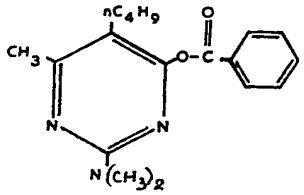


was prepared as follows:— 4-hydroxy-6-methyl-2-morpholino-pyrimidine (4.87 g., 0.025 mole) was suspended in dry dimethylformamide (25 ml.) and to the stirred suspension was added, all at once, 2 ml., 0.025 mole of methane sulphonyl chloride. To the stirred mixture was added, dropwise from a burette, 3.5 ml., 0.025 mole of triethylamine. The temperature of the reaction mixture rose to 42°C., and the mixture became almost clear. Stirring was continued for 2 hours, the solution filtered, and the filtrate was poured into ice-water. The precipitated material was filtered off, washed with a little ice-cold water, and dried. Recrystallisation from ethanol gave the product, 4.05 g. (68%) m.p. 131°C.

The following compounds were also prepared by the method of Example 4.

Compound No.	Physical Characteristic	Solvent of Crystallisation
20	m.p. 138° C.	EtOH
21	m.p. 76° C.	EtOH
24	m.p. 113—114° C.	EtOH

EXAMPLE 5



5 - n - Butyl - 2 - dimethylamino - 4 - methyl - 6 - phenylcarbonyloxypyrimidine, (Compound No. 10, Table I) having the above formula, was prepared as follows:— a mixture of 5-n-butyl-2-dimethylamino-4-hydroxy-6-methylpyrimidine (4.19 g., 0.02 mole), anhydrous potassium carbonate (2.76 g., 0.02 mole), benzoyl chloride (2.81 g., 0.02 mole) and ethyl acetate (50 ml.) was stirred and heated under reflux for 7 hours The reaction mixture was left at room temperature overnight, the solvent removed in vacuo, and the residue taken up in toluene (100 ml.). The toluene was washed with ice-cold 5% aqueous sodium hydroxide solution, then with water until the washings were neutral, and finally dried ($MgSO_4$). Removal of the toluene in vacuo left the product as a white crystalline solid (5.2 g., 83%) which was recrystallized from ethanol, m.p. 59°C.

The above reaction was found to proceed satisfactorily in the solvents benzene, toluene, methyl ethyl ketone and acetonitrile. Ethyl acetate was also a suitable solvent.

In the following Examples the words: "LUBROL", "AROMASOL", "DISPERSOL", "LISSAPOL", "CELLOFAS" are Trade Marks.

EXAMPLE 6

An emulsion concentrate was made up by mixing together the ingredients set out below in the proportions stated and stirring the mixture until all the constituents were dissolved.

Compound No. 10	10%
Ethylene Dichloride	40%
Calcium dodecylbenzenesulphonate	5%
"Lubrol" L	10%
"Aromasol" H	35%

EXAMPLE 7

A composition in the form of grains readily disperisble in a liquid, e.g. water, was prepared by grinding together the first three of the ingredients listed below in the presence of added water and then mixing in the sodium acetate. The reultant mixture was dried and passed through a British Standard mesh sieve, size 44100, to obtain the desired size of grains.

Compound No. 10	50%
"Dispersol" T	25%
"Lubrol" APN5	1.5%
Sodium acetate	23.5%

EXAMPLE 8

The ingredients listed below were all ground together in the proportions stated to produce a powder formulation readily dispersible in liquids.

Compound No. 10	45%
"Dispersol" T	5%
"Lissapol" NX	0.5%
"Cellofas" B600	2%
Sodium acetate	47.5%

EXAMPLE 9

The active ingredient (Compound No. 10 of Table I) was dissolved in a solvent and the resultant liquid was sprayed onto granules of Fuller's earth. The solvent was then allowed to evaporate to produce a granular composition.

Compound No. 10	5%
Fuller's earth or China clay granules	95%

EXAMPLE 10

A composition suitable for use as a seed dressing was prepared by mixing all three of the substituents set out below in the proportions stated.

Compound No. 10	50%
Mineral oil	2%
China clay	48%

EXAMPLE 11

A dusting powder was prepared by mixing, in the proportions stated, the active ingredient with talc.

Compound No. 10	5%
Talc	95%

EXAMPLE 12

A Col formulation was prepared by ball-milling the constituents set out below and then forming an aqueous suspension of the ground mixture with water.

Compound No. 10	40%
"Dispersol"	10%
"Lubrol"	1%
Water	49%

EXAMPLE 13

Formulations similar to those set out in Examples 6—12 above but containing as active ingredient a compound numbered 5, 6, 8, 9, 11 to 13, 27, 28, 35 to 41 respectively, from Table I above, were prepared by methods similar to those described in each particular Example.

Compositions according to the invention were made up in the following manner and tested against various fungal diseases, and the results of these tests are shown in Tables II and III hereinafter. In the tests, both a protectant and an eradicant test were carried out, and in the protectant test the plants were sprayed so that the leaves were wetted with a solution or suspension containing 500 parts per million of the active compound and 0.1% of a wetting agent, and after 24 hours were inoculated with the disease, the extent of which was assessed visually at the end of the test. In the eradicant test, the plants were inoculated with the disease and then sprayed (so that the leaves were wetted) after a number of days depending on the disease with a solution or suspension containing 500 parts per million of the active compound and 0.1% of a wetting agent. The results are shown in Table II below as a grading giving the percentage amount of disease as follows. The time in days stated in the headings to table II is the period in time between spraying of the plant and assessment of the disease.

Grading	Percentage Amount of Disease
0	61 to 100
1	26 to 60
2	6 to 25
3	0 to 5

TABLE II

Compound No. (See Table I above)	PUCCINIA RECONDITA (Rust)		PHYTOPHTHORA-INFESTANS (Late Blight)		SPHAEROTHECA FULIGINEA (Powdery Mildew)		ERYSIPHE GRAMINIS (Powdery Mildew)		ERYSIPHE GRAMINIS (Powdery Mildew)		PODOSPHAERA LEUCOTRICHA (Powdery Mildew)		UNCINULA NECATOR (Powdery Mildew)		PLASMOPARA VITICOLA (Downy Mildew)		PIRICULARIA ORYZAE (Blast)		VENTURIA INAEQUALIS (Scab)	
	Wheat 10 days		Tomato 4 days		Cucumber 10 days		Wheat 10 days		Barley 10 days		Apple 7—14 days		Vine 14 days		Vine 7 days		Rice 7 days		Apple 14 days	
	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad
1	0	0	0	—	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2	0	0	0	—	3	3	3	—	3	—	3	3	1	—	2	—	—	—	0	—
3	0	0	0	—	3	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
4	0	0	1	—	3	3	2	—	2	—	1	—	0	—	0	—	—	—	0	—
5	0	0	2	—	3	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
6	0	0	3	—	3	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
7	0	0	2	—	3	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—
8	1	0	2	—	3	3	3	—	3	—	3	3	3	—	0	—	3	—	0	—
9	1	0	2	—	3	3	3	—	3	—	3	—	1	—	1	—	3	—	0	—
10	2	0	2	—	3	3	3	—	3	—	3	—	3	—	1	—	1	—	0	—
11	0	0	2	—	2	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
12	1	0	3	—	3	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—

TABLE II (Continued)

Compound No. (See Table I above)	Puccinia Recondita (Rust)		Phytophthora-Infestans (Late Blight)		Sphaerotheca Fuliginea (Powdery Mildew)		Erysiphe Graminis (Powdery Mildew)		Erysiphe Graminis (Powdery Mildew)		Podosphaera Leucotricha (Powdery Mildew)		Uncinula Necator (Powdery Mildew)		Plasmopara Viticola (Downy Mildew)		Piricularia Oryzae (Blast)		Venturia Inaequalis (Scab)	
	Wheat 10 days		Tomato 4 days		Cucumber 10 days		Wheat 10 days		Barley 10 days		Apple 7—14 days		Vine 14 days		Vine 7 days		Rice 7 days		Apple 14 days	
	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad
13	0	0	3	—	3	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—
14	—	—	—	—	3	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15	0	0	0	—	3	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
16	1	0	0	—	3	3	2	0	3	—	3	—	1	—	0	—	1	—	0	—
17	0	0	3	—	2	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—
18	0	0	—	—	1	3	0	—	0	—	3	—	2	—	0	—	0	—	3	—
19	1	0	0	—	0	0	1	—	0	—	0	—	1	—	3	—	0	—	1	—
20	1	0	0	—	0	0	1	—	0	—	2	—	0	—	1	—	0	—	0	—
21	2	0	1	—	0	0	0	—	0	—	0	—	0	—	2	—	0	—	3	—
22	0	0	0	—	—	1	0	—	0	—	3	—	0	—	1	—	1	—	1	—
23	0	0	0	—	0	0	0	—	2	—	1	—	1	—	2	—	1	—	0	—
24	0	0	1	—	0	0	1	—	0	—	1	—	0	—	2	—	0	—	0	—
25	0	0	0	—	3	2	3	—	1	—	—	—	—	—	—	—	0	—	—	—
26	0	0	0	—	3	3	1	—	2	—	2	—	0	—	0	—	2	—	3	—

TABLE II (Continued)

Compound No. (See Table I above)	PUCCINIA RECONDITA (Rust)		PHYTOPHTHORA-INFESTANS (Late Blight)		SPHAEROTHECA FULIGINEA (Powdery Mildew)		ERYSIPHE GRAMINIS (Powdery Mildew)		ERYSIPHE GRAMINIS (Powdery Mildew)		PODOSPHAERA LEUCOTRICHIA (Powdery Mildew)		UNCINULA NECATOR (Powdery Mildew)		PLASMOPARA VITICOLA (Downy Mildew)		PIRICULARIA ORYZAE (Blast)		VENTURIA INAEQUALIS (Scab)	
	Wheat 10 days		Tomato 4 days		Cucumber 10 days		Wheat 10 days		Barley 10 days		Apple 7—14 days		Vine 14 days		Vine 7 days		Rice 7 days		Apple 14 days	
	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad	Prot	Erad
27	0	0	0	—	3	2	3	—	3	—	3	—	2	—	1	—	1	—	0	—
28	0	0	1	—	3	3	3	—	3	—	3	—	3	—	2	—	3	—	1	—
29	2	—	1	—	1	0	0	—	2	—	0	—	1	—	0	—	—	—	1	—
30	1	0	1	—	0	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—
33	0	0	1	—	3	3	0	—	0	—	1	—	0	—	2	—	0	—	0	—
34	0	0	1	—	0	3	1	—	0	—	0	—	0	—	0	—	0	—	1	—
35	0	0	0	—	0	2	0	—	1	—	0	—	1	—	1	—	0	—	1	—
36	0	0	1	—	0	1	1	—	0	—	0	—	0	—	0	—	0	—	1	—
37	0	0	—	—	3	3	0	—	2	—	0	—	0	—	0	—	0	—	0	—
38	0	0	—	—	3	3	2	—	3	—	3	—	1	—	0	—	0	—	2	—
39	0	0	—	—	3	3	0	—	1	—	3	—	1	—	0	—	0	—	3	—
40	0	0	—	—	3	3	2	—	1	—	3	—	2	—	0	—	0	—	3	—
41	0	0	1	—	3	3	3	—	2	—	3	—	2	—	0	—	0	—	1	—
44	0	0	0	—	3	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—

The toxicity of a number of the pyrimidine derivatives of this invention towards a variety of insect pests was investigated and the tests conducted and results obtained are set out below. The compounds of the invention were in each case used in the form of a liquid preparation containing 0.1% by weight of the compound. The preparations were made by dissolving each of the compounds in a mixture of solvents consisting of 4 parts by volume of acetone and 1 part by volume of diacetone alcohol. The solutions were then diluted with water containing 0.01% by weight of a wetting agent sold under the trade name of "LISSAPOL" NX until the liquid preparations contained the required concentration of the compound ("LISSAPOL" is a Trade Mark).

The test procedure adopted with regard to each test insect was basically the same and comprised supporting a number of the insects on some medium which may be a host plant or some foodstuff on which the insect feeds, and treating either or both the insect and the medium with the preparations. The mortality of the insects was then assessed at periods varying from one to three days after the treatment.

The results of the tests are given below in Table III. In this Table the first column indicates the compound used. Each of the subsequent columns indicates the name of the test insect, the host plant or medium on which it was supported, and the number of days which were allowed to elapse after treatment before assessing the percentage of insects which had been killed. The assessment is expressed in integers which range from 0 to 3.

0	represents	less than	30%	kill
1	„	from	30—49%	„
2	„	„	50—90%	„
3	„	over	90%	„

The concentration of the invention compound in the solutions used was 1,000 parts per million for all the pests except in the cases of *Aedes aegypti* and *Meloidogyne incognita* when the concentration of the invention compound in the solution used was 100 parts per million.

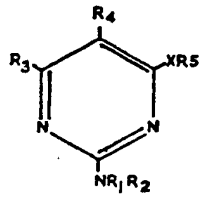
TABLE III

Compound No. (See Table I above)	AEDES AEGYPTI	APHIS FABAE	MACROSIPHUM PISI	TETRANYCHUS TELARIUS	TETRANYCHUS TELARIUS	PHAEDON COCHLEARIAE	MELOIDOGYNE INCOGNITA
	Mosquito larva	Black aphid	Green aphid	Red Spider mite	Red Spider egg	Mustard beetle	Root Knot nematode
	Water	Broad Bean	Broad Bean	French Bean	French Bean	Mustard paper	Water
	—	2 days	2 days	3 days	3 days	2 days	2 days
5	0	2	3	2	0	—	—
6	0	2	3	0	0	—	—
9	0	2	2	0	0	—	—
17	0	2	2	0	0	—	—
19	2	0	0	2	0	—	—
22	1	0	0	2	3	2	—
30	3	1	1	0	0	—	—
35	—	—	2	0	0	—	1
36	3	—	—	—	—	—	3
37	—	—	—	—	—	—	3
38	3	—	—	—	—	—	—
40	2	—	—	—	—	—	—
41	2	—	—	—	—	—	—
45	2	—	—	—	—	—	—

WHAT WE CLAIM IS:—

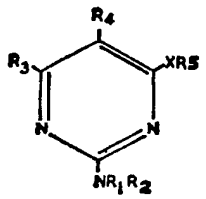
(1) A 2-amino pyrimidine bearing in the 6-position a carboxyl- or sulphonyl-esterified hydroxy or mercapto group, or a salt thereof.

(2) A pyrimidine derivative having the formula:—



or a salt thereof, wherein R_1 and R_2 represent atoms of hydrogen, substituted or unsubstituted hydrocarbon groups, or together with the adjacent N-atom from a heterocyclic ring which may contain one or more additional hetero- atoms; R_3 and R_4 represent atoms of hydrogen or halogen, substituted or unsubstituted hydrocarbon groups or nitro groups; X represents an atom of oxygen or sulphur; and R_5 is a carbonyl or sulphonyl group bearing directly, or through an oxygen or sulphur atom, a substituted or unsubstituted hydrocarbon group, or a heterocyclic group.

(3) A pyrimidine derivative having the formula:—



or a salt thereof, wherein R_1 and R_2 represent hydrogen atoms, lower alkyl radicals, halophenyl radicals, or together with the adjacent nitrogen atom form a piperidino radical, a morpholino radical or a 1-methyl piperazin-4-yl radical; R_3 represents a hydrogen atom, a lower alkyl radical or a phenyl radical; R_4 represents an atom of hydrogen or bromine, a lower alkyl, lower alkenyl, or benzyl radical, or a nitro group; X represents an atom of oxygen or sulphur; and R_5 is a carbonyl or sulphonyl group bearing directly, or through an atom of oxygen or sulphur, a lower alkyl radical, a lower alkenyl radical, a phenyl radical or a nitro-, halo-, lower alkyl-substituted phenyl radical, a piperidino radical, a furyl radical, or a styryl radical.

(4) A pyrimidine derivative as claimed in Claim 2 wherein R_1 and R_2 represent hydrogen, or lower alkyl radicals; R_3 represents hydrogen, a lower alkyl radical or a phenyl radical; R_4 represents an atom of bromine, a lower alkyl, lower alkenyl, or benzyl radical, and R_5 is a carbonyl or sulphonyl group bearing a lower alkyl radical, a lower alkoxy radical, a lower alkylthio radical, a phenyl radical or a nitro-, lower alkyl- or halo-substituted phenyl radical, a phenyl thio radical, an alkenyl radical, an aralkenyl radical or a piperidino or furyl radical; or a salt thereof.

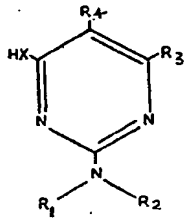
(5) A pyrimidine derivative as claimed in Claim 4 wherein R_1 and R_2 are hydrogen or lower alkyl radicals; R_3 is a lower alkyl radical; R_4 is a lower alkyl radical having 2 to 6 carbon atoms; and R_5 is a carbonyl or sulphonyl group bearing a lower alkyl radical, a lower alkoxy radical, a phenyl radical or a styryl radical.

(6) A pyrimidine derivative according to Claim 5 wherein R_1 and R_2 are both methyl radicals or R_1 is hydrogen and R_2 is an ethyl radical; R_3 is a methyl radical; R_4 is butyl or amyl radical; X is an atom of oxygen; and R_5 is lower alkyl, lower alkoxy or phenyl radical.

(7) Each of the pyrimidine derivatives set out hereinbefore in Table I.

(8) 5 - n - butyl - 2 - dimethylamino - 4 - methyl - 6 - phenylcarbonyloxy-pyrimidine.

(9) A process for making a pyrimidine derivative claimed in any of Claims 1 to 7 which comprises reacting a compound of the formula:—



wherein R_1, R_2, R_3, R_4 and X have any of the meanings stated in Claim 2 with an acyl or sulphonyl halide of the formula:—

$$R_5 \text{ —— Hal}$$

wherein R_5 has any of the meanings stated in Claim 2 and Hal represents a halogen atom under conditions where the hydrogen halide which is formed is removed as it is produced.

(10) A process according to Claim 9 carried out in the presence of a diluent as a reaction medium.

(11) A process according to Claim 10 wherein the diluent is a solvent for the reactants.

(12) A process as claimed in any of Claims 9 to 11 wherein the hydrogen halide is removed by carrying out the reaction in the presence of an acid acceptor.

(13) A process as claimed in Claim 12 wherein the acid acceptor is a base or a salt of a strong base and a weak acid.

(14) A process as claimed in Claim 13 wherein the acid acceptor is an alkali, or alkaline earth metal, hydroxide or carbonate.

(15) A process as claimed in Claim 13 wherein the base is a tertiary amine.

(16) A process as claimed in Claim 15 wherein the tertiary amine is triethylamine.

(17) A process as claimed in Claim 15 wherein the tertiary amine is pyridine.

(18) A process for making a pyrimidine derivative as claimed in any one of Claims 1 to 8, which comprises reacting the appropriate acyl or sulphonyl halide with a metallic salt of the appropriate 6-hydroxy- or 6-mercapto pyrimidine, if necessary in the presence of a solvent.

(19) A pesticidally active composition comprising as active ingredient a pyrimidine derivative as claimed in any of Claims 1 to 8 and a diluent.

(20) A pesticidally active composition as claimed in Claim 19 wherein the diluent is a solid diluent.

(21) A pesticidally active composition as claimed in Claim 20 wherein the solid diluent is an inert substance in powder or granular form.

(22) A pesticidally active composition as claimed in Claim 20 wherein the solid diluent is a powdered or granular fertiliser material.

(23) A pesticidally active composition as claimed in Claim 19 wherein the diluent is a liquid.

(24) A pesticidally active composition as claimed in Claim 23 wherein the liquid is water or an organic solvent.

(25) A pesticidally active composition as claimed in any of Claims 19 to 24 comprising a wetting agent.

(26) A pesticidally active composition as claimed in any of Claims 19 to 25 comprising from 0.001% to 85% by weight of the active ingredient.

(27) A pesticidally active composition as claimed in Claim 26 comprising from 10% to 85% by weight of the active ingredient.

(28) A pesticidally active composition as claimed in Claim 25 comprising from 0.001% to 1.0% by weight of the active ingredient.

(29) A method of combating undesired fungal infections in plants which comprises applying to the locus of the plant a pyrimidine derivative as claimed in any of Claims 1 to 8 or a composition as claimed in any of Claims 19 to 28.

(30) A method of combating undesired insect infestations in plants which comprises applying to the locus of the plant an insecticidally active pyrimidine derivative as claimed in any of Claims 1 to 8 or a composition as claimed in any of Claims 19 to 28 containing such a derivative.

(31) A method of combating plant pathogens which comprises applying to a plant or to seeds thereof, a pyrimidine derivative as claimed in any of Claims 1 to 8 or a composition as claimed in any of Claims 19 to 28.

(32) A method of treating agricultural soil to combat pests on plants comprising applying to the soil a pyrimidine derivative as claimed in any of Claims 1 to 8 or a composition as claimed in any of Claims 19 to 28.

(33) A fertiliser composition comprising a pyrimidine derivative as claimed in any of Claims 1 to 8.

(34) Pyrimidine derivatives and processes for their preparation substantially as described, particularly with reference to the foregoing Examples 1 to 5.

(35) Pesticidally active compositions substantially as described, particularly with reference to the foregoing Examples 6 to 13.

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Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1970.
Published by the Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.